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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/355,220	10/06/1999	THOMAS HASLER	11002/002001	6146

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EXAMINER
GRASER, JENNIFER E

ART UNIT	PAPER NUMBER
1645	16

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/355,220	Applicant(s) Bern et al.
	Examiner Jennifer Graser	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Amendt. B, 8/26/02*

2a)☒ This action is **FINAL.** 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-36* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideratio

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some* c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☐ Notice of References Cited (PTO-892)

16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18)☐ Interview Summary (PTO-413) Paper No(s). _____

19)☐ Notice of Informal Patent Application (PTO-152)

20)☐ Other:

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Acknowledgment and entry of the Amendment submitted 8/26/02, Paper No.15B, has been made. Claims 23-36 are currently pending. The Preliminary Amendment filed 7/23/99 has been located and entered. Amendment to the claims presented in the Preliminary Amendment as requested by Applicant have been made.

The former 102(b) rejections of the claims by Gotschlich et al. and Rienstra et al. have been obviated by the recent amendment and the Preliminary Amendment.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 23-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over in view of over Gotschlich et al. or Schneerson et al (J.Exp. Med. 1980. 152:361-376) in view of Hou et al (J. Parenteral Science and Technology, 1990. 44(4): 204-209) and Lewis.

Gotschlich et al disclose a method of isolating polysaccharides from *N.meningitidis* which comprises using a detergent, Cetavlon, to rapidly precipitate polysaccharides from whole cell culture. Next ethanol is added to the solution and the mixture is centrifuged. The precipitate

is then washed again with ethanol, then twice with acetone to remove the detergent and alcohol. See pages 1350-1351. Schneerson et al teach the isolation of polysaccharides from *H.influenzae* for use in immune compositions. The polysaccharides are isolated by using a detergent, Cetavlon, to rapidly precipitate polysaccharides from whole cell culture. Next ethanol is added to the solution and the mixture is centrifuged. The precipitate is then washed again with ethanol, then twice with acetone to remove the detergent and alcohol.

However, Schneerson and Gotschlich et al do not specifically teach the use of a polymer filter, deep bed filter, or depth filter, for the removal of endotoxins from the isolated polysaccharides.

Hou et al teach a method for removing endotoxins from bacterial polysaccharides using a depth filter or deep bed filter. Hou et al teach that the removal of these endotoxins is important for pharmaceutical purposes. Hou teaches that filtration methods using ultra filtration membranes or depth filters are popular means of depyrogenating biological solutions. The reference teaches that the positively charged depth filer is an effective, economical and practical method for endotoxin removal from large volumes (see page 208). Lewis teaches that depth bed filters can be used to remove endotoxins.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use a depth filter (deep bed filter) with a polymer filter to remove the endotoxins from the polysaccharides isolated by Gotschlich et al. or Schneerson because both Hou teaches that the endotoxins are highly toxic and must be removed from pharmaceutical

products prior to use. Hou teaches that positively charged depth filer is an effective, economical and practical method for endotoxin removal from large volumes (see page 208)

Additionally, the concentrations recited in dependent claims 30-32 are result effective variables. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitations recited in instant claims 30-32 are for any particular purpose or solve any stated problem and the prior art teaches that these concentrations often vary according to the specific sample being purified, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by the prior art by normal optimization procedures.

Response to Applicants' Arguments:

Applicants argue that each step of the prior art references is complete in itself. They argue that the methods of the prior art references are capable of being used to isolate polysaccharides or remove endotoxins without modifying, substituting or adding steps. They

argue that since the cited references are complete in themselves, there is no motivation for the skilled artisan change any of the steps. This has been fully and carefully considered, but is not deemed persuasive. The primary references teach every step except filtering with a deep bed filter. Changing the choice of filters is common in the art and often done to enhance yield and purification of a desired product. Further, the secondary reference, Hou et al., provides motivation in choosing a depth filer for removing endotoxin. Hou et al recite that the positively charged depth filer is an effective, economical and practical method for endotoxin removal from large volumes (see page 208). Hou et al teach that the removal of these endotoxins from polysaccharides is very important for pharmaceutical purposes. Hou et al. teaches other methods of filtration, such as ultrafiltration, but this does not lead away from the choice of a deep bed filter because this passage is only in the Introduction portion of the reference where Hou recognizes that a more economical and convenient means for depryogenating fluids in large volumes is needed. The basis of the article is to explore this new convenient and economical means, i.e., the use of the positively charged depth bed filter. The conclusion of the article, see page 208, states that the positively charged depth filer is an effective, economical and practical method for endotoxin removal from large volumes. It appears that Hou et al. has identified a better alternative to the traditional filters known in the art. Further, the title of the Hou et al. reference is: "Depryogenation by Endotoxin Removal with Positively Charged Depth Filter Cartridge". It cannot be seen how this reference can be teaching away from substituting the use of a deep bed filter in the primary references. Motivation is clearly stated. Lewis does not teach

away from the invention. Lewis was merely cited to demonstrate that deep bed filters were commonly used in the art to remove endotoxins. Taken with the teachings of Hou, one would be clearly motivated to choose a positively charged depth bed filter.

With respect to Applicants' arguments regarding the addition of steps in Gotlisch and Schneerson, the argument is not commensurate with the claimed subject matter. The claims as currently written do not exclude additional steps from being performed, i.e., "wherein the following steps are carried out" is open language allowing for the inclusion of additional steps.

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

4. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is (703) 308-4242 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (703) 308-1742. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JGraser 11/15/04

Jennifer Graser
Primary Examiner
Art Unit 1645